Neonatal infections and neonatal seizures

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objectives

• By the end of this lecture the student should
• Define neonatal sepsis illustrating the causative organism, describing clinical presentation, outline investigation and management.
• In the second part
• Define seizure, classify, differentiate seizure and non seizure disorders, investigate and manage a neonate with seizure
Neonatal Infections

Sepsis       Meningitis
Pneumonia    Otitis Media
Diarrheal Disease
☆ UTI ☆
Osteomyelitis
Suppurative Arthritis
Conjunctivitis
Orbital Cellulitis
Cellulitis - - Omphalitis
Bacterial / Viral / Fungal
Multi-organ involvement common
Neonatal sepsis

• Clinical syndrome of systemic illness accompanied by bacteremia occurring in the first month of life

• Incidence
  – 1-8/1000 live births
  – 13-27/1000 live births for infants < 1500g

• Mortality rate is 13-25%
  – Higher rates in premature infants and those with early fulminant disease
Early Onset

- First 5-7 days of life
- Usually multisystem fulminant illness with prominent respiratory symptoms (probably due to aspiration of infected amniotic fluid)
- High mortality rate
  - 5-20%
- Typically acquired during intrapartum period from maternal genital tract
  - Associated with maternal chorioamnionitis
Late Onset

• May occur as early as 5 days but is most common after the first week of life
• Less association with obstetric complications
• Usually have an identifiable focus
  – Most often meningitis or sepsis
• Acquired from maternal genital tract or human contact
Causative organisms

• Primary sepsis
  – Group B streptococcus
  – Gram-negative enterics (esp. *E. coli*)
  – *Listeria monocytogenes, Staphylococcus*, other streptococci (entercocci), anaerobes, *H. flu*

• Nosocomial sepsis
  – Varies by nursery
  – *Staphylococcus epidermidis, Pseudomonas, Klebsiella, Serratia, Proteus*, and yeast are most common
Risk factors

• Prematurity and low birth weight
• Premature and prolonged rupture of membranes
• Maternal peripartum fever
• Amniotic fluid problems (i.e. mec, chorio)
• Resuscitation at birth, fetal distress
• Multiple gestation
• Invasive procedures
• Galactosemia
• Other factors: sex, race, variations in immune function, hand washing in the NICU
Clinical presentation

- Clinical signs and symptoms are nonspecific
- **Differential diagnosis**
  - RDS
  - Metabolic disease
  - Hematologic disease
  - CNS disease
  - Cardiac disease
  - Other infectious processes (i.e. TORCH)
Clinical presentation

- Temperature irregularity (high or low)
- Change in behavior
  - Lethargy, irritability, changes in tone
- Skin changes
  - Poor perfusion, mottling, cyanosis, pallor, petechiae, rashes, jaundice
- Feeding problems
  - Intolerance, vomiting, diarrhea, abdominal distension
- Cardiopulmonary
  - Tachypnea, grunting, flaring, retractions, apnea, tachycardia, hypotension
- Metabolic
  - Hypo or hyperglycemia, metabolic acidosis
Diagnosis

• Cultures
  – Blood
    • Confirms sepsis
    • 94% grow by 48 hours of age
  – Urine
    • Don’t need in infants <24 hours old because UTIs are exceedingly rare in this age group
  – CSF
    • Controversial
    • May be useful in clinically ill newborns or those with positive blood cultures
Adjunctive lab tests

• White blood cell count and differential
  – Neutropenia can be an important sign
  – Serial values can establish a trend
• Platelet count
  – Late sign and very nonspecific
• Acute phase reactants
  – CRP rises early, monitor serial values
  – ESR rises late
• Other tests: bilirubin, glucose, sodium
Radiology

• CXR
  – Obtain in infants with respiratory symptoms
  – Difficult to distinguish GBS or *Listeria* pneumonia from uncomplicated RDS

• Renal ultrasound and/or VCUG in infants with accompanying UTI
Management

• Antibiotics
  – Primary sepsis: ampicillin and gentamicin
  – Nosocomial sepsis: vancomycin and gentamicin or cefotaxime
  – Change based on culture sensitivities
  – Don’t forget to check levels
Supportive therapy

• Respiratory
  • Oxygen and ventilation as necessary

• Cardiovascular
  • Support blood pressure with volume expanders and/or pressors

• Hematologic
  • Treat DIC with Fresh frozen plasma and/or cryo

• CNS
  • Treat seizures with phenobarbital
  • Watch for signs of SIADH, and treat with fluid restriction

• Metabolic
  • Treat hypoglycemia/hyperglycemia and metabolic acidosis
GBS Prophylaxis

• GBS is the most common cause of early-onset sepsis
  – 0.8-5.5/1000 live births
  – Fatality rate of 5-15%
• 10-30% of women are colonized in the vaginal and rectal areas
• Most mothers are screened at 35-37 weeks gestation
Neonatal seizures

• Seizures are paroxysmal involuntary disturbance of brain function that maybe manifested as Impairment of Consciousness, abnormal motor activity, behavioral abnormality, sensory disturbance or autonomic dysfunction.

• Neonates are at particular risk for seizures because of:
  - Metabolic Disturbances.
  - Toxic.
  - Structural abnormality.
  - Infectious Diseases.
• **types of neonatal seizures**

1. **Focal seizure** which usually involves specific group of muscles secondary to:
   - Structural lesions.
   - Infection.
   - Subarachnoid hemorrhage.

2. **Multifocal seizure** (clonic):
   These seizures are characterized by random clonic movements of limbs. The prognosis is generally good.

3. **Tonic seizures**:
   Divided into general and focal usually associated with eye deviation or apnea and most often seen in premature and carry a poor prognosis.
4- **Myoclonic Seizure:**

the manifestations include synchronous single or multiple slow jerks of upper or lower limbs or both and are associated with diffuse CNS pathology, the prognosis is poor.

5- **Subtle seizure:**

50% of seizures in both term and prematures. usually presented as:

- Excessive salivation.
- Alteration of respiratory rate.
- Blinking.
- Nystagmus.
- Bicycling or pedalic movements
- Change in skin color.
- Apnea due to seizures:
  - Most often has either an:
    - Accelerated or normal heart rate while apnea due to other causes usually associated with bradycardia.
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<table>
<thead>
<tr>
<th>Day</th>
<th>Conditions</th>
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<tbody>
<tr>
<td>Day 1</td>
<td>Traumatic brain injury (subdural, subarachnoid, or intraparenchymal hemorrhages)*</td>
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<td>Hypoxia and ischemia</td>
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<td>Stroke (arterial more likely than venous)</td>
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<td>Infection (bacterial or viral)*</td>
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<td>Severe inborn metabolic disorder (e.g., deficiency of sulfite oxidase or non-ketotic hyperglycinemia)*</td>
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<td>Systemic hypoglycemia*</td>
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<td>Electrolyte disturbance (hypocalcemia or hyponatremia)*</td>
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<td>Intoxication (maternal substance abuse)*</td>
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<td>Day 2</td>
<td>Stroke (especially venous thrombosis)</td>
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<tr>
<td></td>
<td>Traumatic brain injury*</td>
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<td>Inborn metabolic disorder (especially glucose-transporter defect)*</td>
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<td>Day 3</td>
<td>Partial defect in metabolism (e.g., organic acidemias or aminoacidopathies)*</td>
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<td>Benign neonatal convulsions</td>
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<tr>
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<td>Stroke (either arterial or venous)</td>
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<tr>
<td></td>
<td>Withdrawal (from maternal substance abuse)*</td>
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<tr>
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<tr>
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<td>Inborn metabolic disorder*</td>
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* This disorder requires medical or surgical intervention.
### Jitteriness Versus Seizure

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<tr>
<th>CLINICAL FEATURE</th>
<th>JITTERINESS</th>
<th>SEIZURE</th>
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<tbody>
<tr>
<td>Abnormality of gaze or eye movement</td>
<td>O</td>
<td>+</td>
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<tr>
<td>Movements exquisitely stimulus sensitive</td>
<td>+</td>
<td>O</td>
</tr>
<tr>
<td>Predominant movement</td>
<td>Tremor</td>
<td>Clonic jerking</td>
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<tr>
<td>Movements cease with passive flexion</td>
<td>+</td>
<td>O</td>
</tr>
<tr>
<td>Autonomic changes</td>
<td>O</td>
<td>+</td>
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Etiology

1- Hypoxic Ischemic Encephalopathy: 50% to 60%
2- Intracranial hemorrhage:
3- Metabolic problems:
   - hypoglycemia., hypocalcemia., hypomagnesemia.
   - hyponatremia., hypernatremia.
   - pyridoxin deficiency.
   - Disorders of metabolism as phenylketoneurea, hyperglycinemia, urea cycle disorders and $\beta$-alanine abnormalities., organic acidemia.
4- **Infections:**
   - bacterial meningitis.
   - viral infection.
   - toxoplasmosis.
   - syphilis.

5- **Developmental disorders:**
   - cerebral dysgenesis. Neurocutaneous diseases

6- **Drug associated seizures:** narcotic and sedative withdrawal.
7- Polycythemia and hyperviscosity.
8- Familial neonatal seizures.
9- Focal infarction.
10- Hypertensive encephalopathy.
11- Idiopathic.
Etiology

- Clinical history provides important clue
- **Family history** may suggest genetic syndrome
- In the absence of other etiologies, family history of seizures may suggest good prognosis
- **Pregnancy history** is important TORCH infections, diabetes, drugs, fetal distress, preeclampsia or maternal infections
Etiology

- Delivery history
- Type of delivery and antecedent events
- Apgar scores offer some guidance
- Low Apgar score without the need for resuscitation and subsequent neonatal intensive care is unlikely to be associated with neonatal seizures
Etiology

- Postnatal history
- Neonatal seizures in infants without an uneventful antenatal history and delivery may result from postnatal cause. Temperature and blood pressure instability may suggest infection.
Treatment

- Identify the underlying cause:
  - hypoglycemia - D10 solution
  - hypocalcemia - Calcium gluconate
  - hypomagnesemia - Magnesium sulfate
  - pyridoxine deficiency - Pyridoxine
  - meningitis - initiation of antibiotics
Treatment

Anticonvulsant therapy:
- phenobarbital.
- phenytoin.
- lorazepam.
- medazolam.
- diazepam.
Complications

- Cerebral palsy
- Hydrocephalus
- Epilepsy
- Spasticity
- Feeding difficulties
Questions

• Check videos for different types of seizures